

REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments and remarks herein, which place the application in condition for allowance.

Claims 1-4, and 7-22 are pending in the application after entry of the present amendment. Claims 5 and 6 were previously cancelled. Claim 1 has been amended, without prejudice to, or disclaimer of any previously presented subject matter. New dependent claims 9-22 have been added. Support for the new claims is found throughout the specification and in original claim 1. No new matter has been added.

Claim 1 has been amended to remove the recitations “if appropriate” and “in free form” from the claim, to remove the recitation that R_5 is unsubstituted C_1-C_{12} alkyl when R_2 is OR_5 and X is O or S, and to improve the clarity of the claim.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112.

The issues raised by the Examiner in the Office Action are addressed below in the order they appear in the prior Action.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

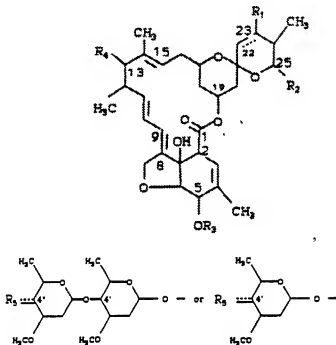
The Examiner has rejected claims 1 and 2 under 35 U.S.C. § 112 second paragraph as allegedly indefinite. The Examiner asserts that the phrases “if appropriate” and “in free form” render the claims indefinite because it is unclear what is appropriate or when it is appropriate, and what constitutes a free form.

Although Applicants disagree with the Examiner, the phrases “if appropriate” and “in free form” have been removed from claim 1, solely to promote prosecution of the application. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 103(a)

The Examiner has rejected claims 1 and 2 under 35 U.S.C. § 103(a) as unpatentable over EP 375393 A1 to Mrozik (Mrozik). Applicants respectfully disagree and traverse the rejection.

The Mrozik describes avermectin derivatives of the formula shown below



wherein R₄ is

Mrozik describes that variable R₅ in the mono- or disaccharide moieties is connected by a single bond when R₅ is amino, loweralkylamino, diloweralkylamino, loweralkanoylamino, loweralkoxycarbonylamino, carbamoyloxy, N-loweralkylcarbamoyloxy, N,N-diloweralkylcarbamoyloxy, loweralkoxy, loweralkanoyloxy, or loweralkoxycarbonyloxy (see page 3, lines 18). When variable R₅ is a carbamoyloxy, N-loweralkylcarbamoyloxy, or N,N-diloweralkylcarbamoyloxy, the 4'- or 4''-position of the compounds is substituted with group -O(CO)NH₂, in which the nitrogen atom may be unsubstituted or substituted with one or two lower alkyl groups. In addition, when variable R₅ in the compounds described by Mrozik is the group loweralkoxycarbonyloxy, the 4'- or 4''-position of the compounds is substituted with the group -O(CO)O-loweralkyl. Lower alkyl is defined as an alkyl group having from 1 to 6 carbon atoms, and no substitution of the lower alkyl is described or suggested (see page 4, lines 20-21).

In contrast to the compounds described by Mrozik, the compounds in the amended claims require that when variable R_2 is $-N(R_3)R_4$, X is O, and R_4 is C_1 - C_{12} alkyl, the alkyl group must be mono- to pentasubstituted by the groups OH, halogen, halo- C_1 - C_2 alkyl, CN, SCN, NO_2 , C_2 - C_6 alkynyl, C_3 - C_8 cycloalkyl which is unsubstituted or substituted by one to three methyl groups; norbornylenyl; C_3 - C_8 cycloalkenyl which is unsubstituted or substituted by one to three methyl groups; C_3 - C_8 halocycloalkyl, C_1 - C_{12} alkoxy, C_1 - C_{12} alkoxy C_1 - C_{12} alkoxy, C_3 - C_8 cycloalkoxy, C_1 - C_{12} alkylthio, C_3 - C_8 cycloalkylthio, C_1 - C_{12} haloalkylthio, C_1 - C_{12} alkylsulfanyl, C_3 - C_8 cycloalkylsulfanyl, C_1 - C_{12} haloalkylsulfanyl, C_3 - C_8 halocycloalkylsulfanyl, C_1 - C_{12} alkylsulfonyl, C_3 - C_8 cycloalkylsulfonyl, C_1 - C_{12} haloalkylsulfonyl, C_3 - C_8 halocycloalkylsulfonyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, $-N(R_6)_2$, $-C(=O)R_7$, $-O-C(=O)R_8$, $-NHC(=O)R_7$, $-S-C(=S)R_8$, $-P(=O)(OC_1-C_6alkyl)_2$, $-S(=O)_2R_{11}$; $-NH-S(=O)_2R_{11}$, $-OC(=O)-C_1-C_6alkyl-S(=O)_2R_{11}$; aryl, benzyl, heterocyclyl, aryloxy, benzyloxy, heterocyclyloxy, arylthio, benzylthio, heterocyclylthio; and also aryl, heterocyclyl, aryloxy, benzyloxy, heterocyclyloxy, arylthio, benzylthio or heterocyclylthio.

Similarly, the amended claims also require that when X is O, R_2 is OR_5 , and R_5 is C_1 - C_{12} alkyl (corresponding to an alkoxy-carbonyloxy in the definition of R_5 in Mrozik), the alkyl group must be mono- to penta substituted the same group of substituents.

The compounds described by Mrozik are not encompassed by the claims as amended. Furthermore, the compounds recited in the amended claims are not described or suggested by Mrozik because they require that when X is O and the variable R_2 is $-N(R_3)R_4$ or OR_5 , and R_4 or R_5 are C_1 - C_{12} alkyl, the alkyl groups must be substituted by at least one of the substituents recited in claim 1. Mrozik only describes compounds having unsubstituted carbamoyl or N-loweralkylcarbamoyl or loweralkoxy-carbonyloxy groups at the 4'- or 4''-positions of the compounds that contain unsubstituted lower alkyl groups. Furthermore, Mrozik provides no suggestion that the loweralkyl groups in the compounds may be substituted or provides any motivation for one of skill in the art to include alkyl groups bearing one or more of the required substituents recited in the instant claims.

Applicants respectfully submit that it is well accepted that the art of biologically active compounds is not generally predictable. There are many examples in the art, where small changes in the substituents of molecules can lead to significantly different steric and electronic properties which may have a significant impact on the activity of the compounds. For example,

small changes in biologically active compounds can affect the binding affinity to a desired receptor or result in a modified toxicity profile.

The compounds recited in the amended claims are substantially different than the compounds described by Mrozik because they require that when variables R_4 and R_5 are C_1 - C_{12} alkyl, the alkyl groups must contain one of the specific substituents recited in claim 1. The nature of the required substituents can significantly change the properties of the compounds because of their polar, electronic and steric contribution to the parent compound. Such modifications distinguish the compounds recited in the amended claims from compounds described by Mrozik, and would be expected to confer different properties to the compounds, particularly with respect to biological activity. In the absence of any teaching or suggestion, one of skill in the art would not be motivated to make the compounds recited in the claims based on the disclosure of Mrozik because they would not have a reasonable expectation that the distinct compounds would retain their potent biological activity against pests and their acceptable safety profile in warm-blooded animals, fish and plants.

In view of the foregoing, it would not have been obvious to one of ordinary skill in the art, at the time of the instant invention to arrive at the compounds and compositions recited in the claims based on the teaching of Mrozik. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) is respectfully requested.

CONCLUSION

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the remarks and amendments herein, and prompt issuance of a Notice of Allowance is respectfully requested.

If the Examiner believes any informalities remain in the application, which may be corrected by Examiner's amendment, or whether any other issues can be resolved by telephone interview, a telephone call with the undersigned is courteously solicited.

The Examiner is authorized to charge any deficiency to Deposit Account No. 50-2354.

Respectfully submitted,
MERIAL LTD.

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